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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,214	01/09/2001	Kenji Yamashita	Q62578	4067

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EXAMINER
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EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 08/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/756,214

Applicant(s)

YAMASHITA ET AL.

Examiner

G. R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 27 and 29-32 is/are pending in the application.
- 4a) Of the above claim(s) 31 and 32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 27, 29 and 30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/254,170.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

#### DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's remarks filed 5/21/04 have been entered.
2. Claims 27 and 29-32 are pending.
3. Claims 31 and 32 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected species of the elected invention.
4. Upon reconsideration and in view of the instant remarks, all previous rejections have been withdrawn. Accordingly, many of Applicant's arguments have been rendered moot. As appropriate, Applicant's remarks of 5/21/04 will be addressed.
5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
  - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
6. Claims 27, 29, and 30 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U. S. Patent No. 6,171,799 (of record) in view of Schwarz et al. (1995, of record), Chavin et al. (1994), Chavin et al. (1993), and Jones et al. (1992).

The '799 patent teaches a culture device for the culturing of immunosuppressive (suppressor) cells, with an affinity for protein, wherein prior to cell culturing the culture device is coated with an anti-CD3 antibody (OKT3) (see particularly column 33, lines 30-53).

The reference differs from the claimed invention in that it does not teach a device further coated with an F(ab)<sub>2</sub> fragment of the anti-CD2 antibody TS2/18 antibody produced by the hybridoma HB195.

Schwarz et al. teaches the culture of T cells with the anti-CD2 TS2/18 antibody and that said culture results in inhibitory effects on T cell activation (see particularly page 5816, column 1, paragraph 4). The reference further teaches that the epitope recognized by TS2/18 is a candidate for CD2-directed immunosuppression (see particularly page 5817, column 2, paragraph 3).

Chavin et al. (1994) teaches that anti-CD2 antibodies can be used to generate Th2 suppressor cells (see particularly Results, *Anti-CD2 mAb induces suppressor cells*) and that various anti-CD2 antibodies are interchangeable (see particularly the sentence spanning pages 3729 and 3730).

Chavin et al. (1993) teaches that anti-CD2 and anti-CD3 antibodies synergize in an immunosuppression context (see particularly Discussion, column 1, second paragraph).

Jones et al. teaches the interchangeability of whole antibodies and F(ab)<sub>2</sub> fragments for the coating of devices (plastic plates) for the incubation of lymphocytes (see particularly page 236, column 1, second paragraph). The reference further teaches that in some situations an F(ab)<sub>2</sub> fragment is preferable, such as when the reduction of a background signal is desirable, (see Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a culture device for the culturing of immunosuppressive (suppressor) cells, wherein prior to cell culturing the culture device is coated with an anti-CD3 antibody, as taught by the '799 patent, additionally coating the plate with a an anti-CD2 TS2/18 antibody, as taught by the Schwarz et al., employing either the whole antibody or an F(ab)<sub>2</sub> fragment of said antibody, given the fact that whole antibodies and F(ab)<sub>2</sub> fragments are interchangeable and in some situations an F(ab)<sub>2</sub> fragment is preferable, as taught by Jones et al. One of ordinary skill in the art would have been motivated to double-coat (anti-CD2 and anti-CD3) the plate given the teachings of Chavin et al. (1994) that anti-CD2 antibodies can be used to generate Th2 suppressor cells and that various anti-CD2 antibodies are interchangeable

and Chavin et al. (1993) that anti-CD2 and anti-CD3 antibodies can synergize in an immunosuppression context. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205USPQ 1069, 1072 (CCPA 1980) (see MPEP 2144.06). Thus, the combination of antibodies would be obvious.

In the remarks filed 5/21/04 Applicant argues that the Examiner had failed to provide adequate motivation to combine the teachings of the '799 patent and Schwarz et al., "Specifically, Applicants submit that OKT3 and TS2/18 are not used for the same purpose in the cited prior art, contrary to the Examiner's position." Applicant further describes the details of the mechanisms of the activity of the anti-CD antibody of Schwarz et al.

It is the Examiner's position that the Chavin et al. references provide sufficient motivation to combine the references, i.e., anti-CD2 antibodies can induce suppressor cells, and anti-CD2 and anti-CD3 antibodies can synergize in an immunosuppression context. Applicant's further arguments regarding the mechanisms of the activity of the anti-CD2 antibody of Schwarz et al. cannot overcome the teachings of the Chavin et al. references which teach the interchangeability of anti-CD2 antibodies.

Applicant argues "unexpectedly superior properties".

It is the Examiner's position that the properties of the instant invention cannot be considered to be unexpected given the teachings of Chavin et al. (1993) that anti-CD2 and anti-CD3 antibodies have been shown to synergize in an immunosuppression context.

7. Claims 27, 29, and 30 are rejected under 35 U.S.C. § 103(a) as being unpatentable over EP 0421380A1 (1990) in view of Schwarz et al. (1995, of record), Chavin et al. (1994), Chavin et al. (1993), and Jones et al. (1992).

EP 0421380A1 teaches a culture device (see particularly page 4, line 16) coated with an anti-CD3 antibody and an anti-CD2 antibody (see particularly page 3, lines 26-27) including an

enzymatically cleaved antibody fragments (see particularly page 3, lines 33-36).

The reference differs from the claimed invention in that it does not teach the specific anti-CD2 antibody TS2/18 produced by the hybridoma HB195 nor the use of an F(ab)<sub>2</sub> fragment.

Schwarz et al. teaches the well known anti-CD2 antibody TS2/18 produced by the hybridoma HB195 (see particularly Abstract)).

Chavin et al. (1994) teaches that anti-CD2 antibodies can be used to generate Th2 suppressor cells (see particularly Results, *Anti-CD2 mAb induces suppressor cells*) and that various anti-CD2 antibodies are interchangeable (see particularly the sentence spanning pages 3729 and 3730).

Chavin et al. (1993) teaches that anti-CD2 and anti-CD3 antibodies synergize in an immunosuppression context (see particularly Discussion, column 1, second paragraph).

Jones et al. teaches the interchangeability of whole antibodies and F(ab)<sub>2</sub> fragments for the coating of devices (plastic plates) for the incubation of lymphocytes (see particularly page 236, column 1, second paragraph). The reference further teaches that in some situations an F(ab)<sub>2</sub> fragment is preferable, such as when the reduction of a background signal is desirable, (see Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a culture device coated with an anti-CD3 antibody and an anti-CD2 antibody, given the teachings of Chavin et al. (1994) that anti-CD2 antibodies can be used to generate Th2 suppressor cells and that various anti-CD2 antibodies are interchangeable and Chavin et al. (1993) that anti-CD2 and anti-CD3 antibodies synergize in an immunosuppression context, including an enzymatically cleaved fragments of an anti-CD2 antibody as taught by EP 0421380A1, employing the TS2/18 anti-CD2 antibody produced by the hybridoma HB195, as taught by Schwarz et al, because the TS2/18 anti-CD2 antibody was well known and readily available, employing either the whole antibody or an F(ab)<sub>2</sub> fragment of said antibody, given the fact that whole antibodies and F(ab)<sub>2</sub> fragments are interchangeable and in some situations an F(ab)<sub>2</sub> fragment is preferable, as taught by Jones et al.

In the remarks filed 5/21/04 Applicant argues that the Examiner had failed to provide adequate motivation to combine the teachings of the EP 0421380A1 and Schwarz et al. and that the combination of the invention provides unexpectedly superior properties.


New motivation to combine as well as a discussion of the asserted unexpected properties of the instant combination of antibodies has been provided as set forth in the rejection and discussed in Section 5 above.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

10. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.

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8/3/04  
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